monosaccharide and a derivative thereof, a disaccharide, and a derivative thereof, an oligosaccharide and a derivative thereof, and a polysaccharide and a derivative thereof.

Please add the following new claims

82. (New) The glucose sensor in accordance with claim 55, further comprising a at least one stabilizer selected from the group consisting of a metal salt, an organic acid, a protein, and a sugar and a derivative thereof.

83. (New) The glucose sensor in accordance with claim 55, wherein the response of the sensor to glucose within the concentration range of 0 to 500 mg/dl is substantially linear after long term preservation.

REMARKS

Initially Applicant acknowledges the courtesy extended by the Examiner in charge of the subject application in holding an interview to discuss the various rejections and the cited art in the Office Action, as reflected in the Interview Summary of 3 April 2003.

Claims 5-83 are currently pending in the present application, of which claims 82-83 are new. Applicant further acknowledges, with appreciation, the indication that claims 5-19, 22-36, and 39-53 are allowable. Accordingly, claims 20, 21, 37-38, 54-83 are currently under consideration and the remarks herein address only the rejections/objections to those claims.

The claims have been amended to correct for minor typographical errors and to more distinctly claim the invention. In particular, claim 38 has been amended to delete the comma between "maleic" and "acid". Claim 56 has been amended to correctly recite the symbols for calcium chloride.

Claim 55 has been amended to delete the requirement that a stabilizer is contained in the reaction layer and also to make clear that the various listed components are an additive rather than a buffer. The requirement of the stabilizer in the reaction layer is now found in new claim 82 and claims 56-59 have been amended to depend from claim 82. Due to the nature of these amendments, it is respectfully submitted that no new matter has been added to the application. Entry of these amendments are respectfully solicited.

Claims 82-83 have been added. Claim 82 recites that the reaction layer further contains a stabilizer, as originally described in claim 55. Claim 83 recites that the response to the glucose sensor within a concentration range of 0-500 mg/dl is substantially linear after long term preservation. Support for this claim can be found throughout the detailed application as, for example, on page 21, beginning on line 2, where Applicant describes highly responsive sensors demonstrating satisfactory linearity. Figures 4-11 illustrate the substantial linear response of these glucose sensors to glucose within the concentration range of 0 to 500 mg/dl. Accordingly, it is respectfully submitted that the addition of these claims do not add new matter to the application. Entry of these claims are respectfully solicited.

The specification has been amended to replace the term "colicin" with "collidine". As discussed below, "collidine" was incorrectly translated into colicin from the Japanese priority application. Support for the term "collidine" is found through out the original priority document. Accordingly, it is respectfully submitted that no new matter has been added to the application by this correction.

Objection to Claim 38

Claim 38 was objected to because of a typographical error. Applicant has corrected claim 38, as suggested by the Examiner. Accordingly, reconsideration and withdrawal of the objection are respectfully solicited.

Rejection Under 35 USC 112

Claims 20, 21, 37, 38, 54 and 55-81 were rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification. In particular, the Examiner rejected the inclusion of "collidine" as a substitute for "colicin" for the rejected claims. Applicant traverses the rejection and respectfully submits that collidine was originally described in the Japanese priority application and, hence, is not new matter.

The present application claims priority to and corresponds to Japanese Application No. 11-212703. Applicant has provided herewith a Rule 132 Declaration by Mr. Koichi Naka ("Naka Decl.") certifying that the term collidine is described in the Japanese language priority application. According to the Naka Declaration, the Japanese priority application lists collidine among the compounds that can be added to a reaction layer of a glucose sensor in paragraphs 0007, 0008, 0009, 0011, 0030, as well as in claims 1, 3, and 4 and in Table 1 of the Japanese language priority application. (Naka Decl. ¶ 3) The terms collidine and colicin are similar in their appearance in the Japanese language (Naka Decl. ¶ 4) and was likely the reason why collidine was incorrectly translated as colicin into the English language. Accordingly, it is respectfully submitted that the original priority application described collidine as a compound that can be added to a reaction layer. Hence, the correction to the present application by substituting collidine for colicin is supported by the

priority document. Reconsideration and withdrawal of the rejection are respectfully solicited.

Rejection of Claims 21 and 38 Under 35 USC 103

Claims 21 and 38 were rejected under 35 USC 103(a) as being unpatentable over Heisei 10-227755 in view of Maslinska-Solich. The rejection is traversed and it is respectfully submitted that the claims are patentable within the meaning of 35 USC 103(a).

Claim 21 recites a method of stabilizing glucose dehydrogenase for use in glucose sensors by the addition of one of several additives including maleic acid. Claim 38 relates to a glucose dehydrogenase composition where one of the additives included in the composition can be maleic acid.

In applying the cited art, the Examiner asserted that paragraph 0007 of the Heisei reference teaches that maleic acid can be added to a reaction layer. Applicant respectfully disagrees with this interpretation of the Heisei reference.

In paragraph 0007, Heisei provides examples of hydrophilic macromolecules. Maleic acid and anhydride are not a macromolecules. Those skilled in the art would understand that the listing of maleic acid or anhydride as such is in error. Applicant has provided herewith a Declaration by one of the inventors to the Heisei reference who is also an inventor to the present application, Mr. Toshihiko Yoshioka ("Yoshioka Decl.").

According to the Yoshioka Declaration, the listing of maleic acid or an anhydride as an example of a hydrophilic macromolecule is not correct and one skilled in this art would recognize that the listing of maleic acid or anhydride as a hydrophilic macromolecule in a reaction layer is in error. (Yoshioka Decl. ¶ 6). As would be understood by those skilled in

the art, hydrophilic macromolecules relate to large molecules such as polymers. Examples of hydrophilic macromolecules (or polymers) are provided in the present application on pages 11 and 12. See, e.g., Yoshioka Decl. ¶ 7. As one skilled in the art would understand, it is the polymeric form of maleic anhydride or acid thereof which is being disclosed in the Heisei reference. (Yoshioka Decl. ¶ 8).

The secondary reference, Maslinska-Solich, does not cure the deficiencies of the primary reference. The secondary reference, in fact, discloses polymeric maleic anhydride, and not its monomeric form as suggested by the Examiner. Hence, there is no way to combine the secondary reference and the primary reference to arrive at claims 21 or 38.

Based on the foregoing, it is respectfully submitted that the combination of references do not negate the patentability of claims 21 and 38. Reconsideration and withdrawal of the rejection are respectfully solicited.

Rejection of Claims 55 and 59-63 Under 35 USC 103

Claims 55 and 59-63 were rejected under 35 USC 103(a) as being unpatenable over Crismore in view of Vetter and Gotoh. The rejection is traversed and it is respectfully submitted that these claims are patentable within the meaning of 35 USC 103(a).

Independent claim 55 relates to a glucose sensor. This sensor comprises an electrically insulating base plate and an electrode system which includes a reaction layer. The reaction layer contains a glucose dehydrogenase whose co-enzyme is pyrrolo-quinoline quinone, and an additive selected from various compounds including citric acid or a citrate salt.

Crismore teaches electrochemical biosensor test strips that include succinic acid. There is no mention whatsoever of citric acid or a citrate within the Crismore reference.

To cure this deficiency, the Examiner relies on Vetter. However, the reliance on Vetter is misplaced. Vetter relates to an optical sensor. (See, e.g., column 5, lines 62-65). There is no discussion within Vetter as to the purpose or function of any of the components of the composition. Hence there is no reason why one of ordinary skill in the art would modify the electrochemical biosensor of Crismore with the composition for an optical sensor, as described by Vetter, since Vetter is silent as to the purpose or function of the components of its composition.

Gotoh does not cure the deficiencies of Crismore or Vetter. Gotoh relates to a completely different enzyme, a glucose oxidase (GOD) enzyme. Gotoh has nothing to do with the problems associated with stabilizing a glucose dehydrogenase sensor or compositions thereof. Hence, Applicant respectfully submits that the Examiner in charge of the subject application has not set forth a proper *prima facie* case of obviousness.

Nevertheless, Applicant has provided herewith a Rule 132 Declaration by inventor Keiko Yugawa ("Yugawa Decl."). As reported in the Yugawa Decl., several experiments were carried to compare the effect of succinic acid to sodium citrate in a glucose sensor. (Yugawa Decl. ¶ 4) The data from that comparison shows succinic acid and sodium citrate have significant differences when used as an additive in a reaction layer of a glucose sensor. (Yugawa Decl. ¶ 5-8) For example, the glucose sensor prepared with sodium citrate maintains substantially the same response when used either initially after fabrication or after an accelerated aging. Applicant respectfully submits that the evidence provided through the Yugawa Declaration shows that the use of succinic acid and citric acid are not

equivalent. Further, the Yugawa Declaration provides evidence that a sensor made with sodium citrate is more accurate and reliable over time than one made from succinic acid. This result is not suggested or recognized by the cited art. Hence, any *prima facie* case of obviousness, which the Examiner believes has been established, has now been rebutted by the Yugawa Declaration.

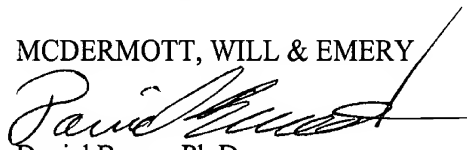
Based on the foregoing, it is respectfully submitted that the application is now in condition for allowance. Reconsideration of the evidence provided herewith and allowance of the application are respectfully solicited.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

MCDERMOTT, WILL & EMERY



Daniel Bucca, Ph.D.
Registration No. 42,368

600 13th Street, N.W.
Washington, DC 20005-3096
(202) 756-8000 DB:MWE
Facsimile: (202) 756-8087
Date: April 21, 2003

#24 attach

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The specification has been amended as follows:

Lines 1-17 on page 5 have been amended as follows:

The glucose sensor in accordance with the present invention comprises an electrically insulating base plate, an electrode system including at least a working electrode and a counter electrode formed on the base plate, and a reaction layer which is formed in contact with or in the vicinity of the electrode system and contains at least PQQ-GDH, wherein the reaction layer further contains at least one additive selected from the group consisting of phthalic acid, a phthalate, maleic acid, a maleate, succinic acid, a succinate, triethanol amine, a triethanol amine salt, citric acid, a citrate, dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole, and ~~colicin~~ collidine.

Lines 1-9 on page 5 and lines 1-4 on page 6 have been amended as follows:

The present invention also relates to a method for stabilizing glucose dehydrogenase for use in glucose sensors, wherein at least one additive is added to PQQ-GDH, the additive being selected from the group consisting of phthalic acid, a phthalate maleic acid, a maleate, succinic acid, a succinate, triethanol amine, a triethanol amine salt, citric acid, a citrate, dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a

tris(hydroxymethly)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole, and ~~colicin~~ collidine.

Lines 1-13 on page 6 have been amended as follows:

The present invention further relates to a glucose dehydrogenase composition for use in glucose sensors, the composition containing PQQ-GDH and at least one additive selected from the group consisting of phthalic acid, a phthalate, maleic acid, a maleate, succinic acid, a succinate, triethanol amine, a triethanol amine salt, citric acid, a citrate, dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole, and ~~colicin~~ collidine.

Lines 24-28 on page 9 and lines 1-14 on page 10 have been amended as follows:

The additive from which the above-mentioned effects can be expected may be exemplified as phthalic acid, a phthalate such as potassium hydrogen phthalate, maleic acid, a maleate such as sodium maleate, succinic acid, a succinate such as sodium succinate, triethanol amine, a triethanol amine salt such as triethanol amine hydrochloride, citric acid, a citrate such a monopotassium citrate, calcium citrate, tripotassium citrate, trisodium citrate, trilithium citrate, diammonium hydrogen citrate, disodium hydrogen citrate, sodium citrate, diammonium citrate, potassium dihydrogen citrate, sodium dihydrogen citrate, disodium citrate or magnesium citrate, dimethyl glutaric acid, (2-N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate,

tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt such as tris(hydroxymethyl)aminomethane hydrochloride, imidazole, and ~~colicin~~ collidine.

Table 1 on page 23 has been amended as follows:

Buffer solution	pH	Residual activity (%)
Potassium hydrogen phthalate	6.0	100
Maleic acid	6.5	100
Succinic acid	6.0	100
Triethanol amine	7.0	100
Sodium dihydrogen citrate	6.5	100
Dimethyl glutaric acid	6.5	100
Tricine	7.5	95.4
Imidazole	7.5	100
~~Colicin~~ Collidine	6.5	96.1
Tris hydrochloride	7.5	63.4
Potassium phosphate	6.5	44.3

IN THE CLAIMS

The claims have been rewritten as follows:

38. (Three Times Amended) A glucose dehydrogenase composition for use in glucose sensors, said composition containing glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone, and at lease one additive selected from the group consisting of phthalic acid, a phthalate, maleic[,] acid, a maleate, triethanol amine, a triethanol amine salt, dimethyl glutaric acid, (N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine

salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole or collidine.

55. (Twice Amended) A glucose sensor comprising an electrically insulating base plate, an electrode system including at least a working electrode and a counter electrode formed on said base plate, and a reaction layer which is formed in contact with or in the vicinity of said electrode system wherein said reaction layer contains: [at least one stabilizer selected from the group consisting of a metal salt, an organic acid, a protein, and a sugar and a derivative thereof;] a glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone; and [a buffer] an additive selected from the group consisting of maleic acid, a maleate, triethanol amine, a triethanol amine salt, citric acid, a citrate, dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole or collidine.

56. (Amended) The glucose sensor in accordance with claim [55] 82, wherein said stabilizer is a metal salt selected from the group consisting of a calcium salt, [CaC_2] $CaCl_2$, a strontium salt and a manganese salt.

57. (Amended) The glucose sensor in accordance with claim [55] 82, wherein said stabilizer is an organic acid selected from the group consisting of α -

ketoglutaric acid, malic acid, fumaric acid, gluconic acid, cholic acid and deoxycholic acid.

58. (Amended) The glucose sensor in accordance with claim [55] 82, wherein said stabilizer is a protein selected from the group consisting of bovine serum albumin, egg albumin and gelatin.

59. (Amended) The glucose sensor in accordance with claim [55] 82, wherein said stabilizer is a sugar or a derivative thereof selected from the group consisting of a monosaccharide and a derivative thereof, a disaccharide, and a derivative thereof, an oligosaccharide and a derivative thereof, and a polysaccharide and a derivative thereof.